COMMENTS ON THE DISCUSSION DRAFT: "PROPOSALS TO INCREASE THE AVAILABILITY OF APPROVED ANIMAL DRUGS FOR MINOR SPECIES AND MINOR USES"

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Submitted by Dr Robert D Armstrong on behalf of Salmon Health to:

Center for Veterinary Medicine
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Salmon Health is providing comments on this discussion draft for three reasons:

1. Salmon Health receives support from the Maine Aquaculture Association (MAA), and development of improved approaches to minor use drug approval will benefit the MAA.

2. The discussion draft proposals address the issue of international harmonization, and progress toward international harmonization has the potential to increase the interest of drug manufacturers in developing safe and effective products for the aquaculture market in both Canada and the United States.

3. Salmon Health receives support from Canadian salmon producers who also face problems with lack of available safe and effective drugs, and the Canadian government has made a committment to consider the success of minor use drug approval initiatives in the United States.

COMMENTS ON THE PROPOSAL INTRODUCTION

The proposal states:

"For this reason, no single proposal is likely to have a significant effect on the problem as a whole. Neither is it likely that any single proposal affecting a given constituent group will have a profound benefit for that group."

Salmon Health concurs that this is a key point, and that US authorities should not expect to resolve the problem by selecting a few individual options from within this proposal. It must be recognized that multiple changes in policies, regulations and legislation are required to bring about a solution.

The proposal introduction recognizes a key problem created by the lack of minor use drug approvals:

"Another reason for concern occurs because commercially valuable minor species-derived food, fiber, or other types of products may not be able to compete with imported products."

The importance of this factor should not be underestimated. For example, aquaculture entrepreneurs will consider their ability to manage business risks in selecting an appropriate location and country for their investment in production facilities. Lack of approved drugs for managing health problems is a potentially unacceptable business risk that acts as a major disincentive against investment in the industry in the U.S. Therefore, the economic cost of failure to resolve the minor use problem is far greater than can be estimated by assessing the economic impacts that lack of treatment options have on established production operations.

An additional obstacle to submission of supplemental applications for aquaculture products that should be noted is that aquatic uses frequently require different formulations than those available through the major use species NADA formulations.

COMMENTS ON PROPOSALS TO INCREASE THE NUMBER OF APPROVED ANIMAL DRUGS FOR MINOR USE

A. MODIFICATION OF EXTRALABEL PROVISIONS

o Will the proposed modification of extralabel provisions and suggested sunset period provide adequate and appropriate temporary relief until approved products are made available, or will it serve as a disincentive to the pursuit of approvals?

The proposed modification will provide temporary relief for some aspects of the lack of approved drug availability by permitting extralabel treatment of a range of aquaculture species with the few drugs now approved. A ten year fixed sunset period is not an adequate time period, and alternatives must be considered to this proposal. The introduction to these draft minor use proposals recognized that few minor use drugs have received approval in the past thirty years despite the support received through various programs. The approval process requires considerable time - it is not unusual for a major use NADA to take seven years with full drug manufacturer support. A more positive approach would be to develop an interactive process that introduced a sunset provision if no further initiatives toward NADA completion were being undertaken. This sunset approach would also serve as an effective counteracting process in response to any concerns regarding disincentives that may be creat! -
ed for product approval.

o Should the proposed modifications be extended to include reproductive hormones and implants?

Use of reproductive hormones and implants should be included in the proposed modifications. The only rationale for excluding these drugs would be a clear and specific human safety concern regarding a particular drug, and this concern should apply to all drugs. The particular drug could then be removed from the minor use proposals, as has been done with specific drugs under the

new extra label use measures.

B. REMOVAL OF DISINCENTIVES

o Will the suggested strategies be sufficient to remove the existing direct regulatory disincentives?

Increased enforcement resources will be beneficial if these are specifically targeted at the obstacles to minor drug use approval. The most effective way to achieve this will be for FDA/CVM to work closely with representatives of drug manufacturers and minor use producers organizations in undertaking enforcement actions.

C. ENHANCEMENT OF EXISTING PROGRAMS FOR DATA DEVELOPMENT

o Are there additional existing congressional research funds which could be expanded for minor use research?

Additional programs that could be expanded in this area are the Small Business Innovative Research (SBIR) and Sea Grant research funds. There may be other options that should be considered under the USDA research support budget.

o Would the proposed model program provide a useful supplement to the existing NRSP-7 program?

The NRSP-7 is a very valuable initiative, and it would be a shame to dilute this initiative by creation of other similar research programs. A better approach would be to increase the resources available through the NRSP-7 initiative.

o Would the proposed database be useful to parties interested in furthering the approval of minor use products? If so, how might it be developed most cost-effectively?

The proposed data base would not be the best approach to managing this issue. Data on disease problems are best maintained by the producer associations rather than CVM. CVM should concentrate on its area of expertise which is scientific information on drugs. Therefore, a more effective approach would be to develop an electronic database, available through the world wide web, that would permit downloading of public data regarding specific active ingredients identified as priorities for minor use drug approvals. This activity should include an initiative to identify data from all published resources within the world wide body of scientific knowledge on minor species drug pharmacokinetics, safety and efficacy.

D. INCENTIVES TO PURSUE MINOR USE DRUG APPROVALS

o Is the benefit of extended exclusivity, with respect to fostering initial approval, more important than the risk of increased drug costs that could be associated with decreased competition from generic approvals?

There is no question that the benefit of fostering approval is more important than the economic costs of approved drugs. Remember that the lack of approved products for the food animal production industry is an economic issue. If an approved drug is subsequently priced beyond its economic benefit to producers then it will not sell. Therefore, there is a price limit set by the market that the manufacturer cannot exceed. The producer will be better off by having this safe and effective drug available within this price limit, than by having no approved drug under the status quo.

o Would it be a more significant incentive to provide for an extended period of exclusivity for all the claims of the product?

It would be a more significant incentive.

E. DATA SHARING BY MAJOR SPECIES NADA HOLDERS

o Is it fair to require the sharing of data?

It is fair to require the sharing of data where:

1 the data owner is not interested in the market that will be developed through use of the data, and

2 use of the data will not permit a competitor to more easily enter a market that the data owner is interested in.

Under this scenario, sharing the data will not harm the owner, but will benefit other sponsors. To achieve this end, the data owner must first be given the option of extending their label to address the minor use, with the recognition that where the owner chooses not to take this option, then the data can be used to support the minor use drug approval initiative of another organization. The latter organization should not be permitted access to the specific study results in the data, but should be aware of the types of studies contained in the data package.

o How could potential liability be ameliorated under such a data sharing system?

Liability should clearly not fall on the original data owner. One solution would be for minor use producer associations to develop liability coverage as has been developed in the field of minor use crop pesticide approval in some states.

F. CREATION BY STATUTE OF A "MINOR USE ANIMAL DRUG" PROGRAM

o Are the incentives associated with this strategy a necessary component of the overall proposed "Minor Use Animal Drug Program"?

These incentives will be a useful but not necessary component of the overall proposed program. Key challenges in this strategy will be ensuring that the "Minor Use Animal Drug" program

identifies and responds to the appropriate priority needs. To achieve this result, the program will have to work closely with producer associations. This could be achieved through creation of an industry advisory committee to work with the minor use program leaders and provide advice to staff through a structured format and regular meetings.

G. CONDITIONAL DRUG APPROVAL FOR MINOR USES INVOLVING NON-FOOD ANIMALS

o Would the proposed constraints upon conditional approval provide sufficient consumer protection and still provide adequate incentive to pursue a conditional drug approval to final approval?

It is not clear which consumers are to be protected by these constraints, considering that the conditional approvals are for non-food animal use only.

o Is the proposed process appropriately restricted to minor uses involving non-food animals?

It should be an objective to develop the conditional approval process in a manner that permits its use for minor use drugs for food animals also. In particular, where a product has a complete human food safety package through a major use NADA, the conditional approval approach may be a more effective option for facilitating label expansion to a minor species than the extralabel approach.

H. ALTERNATE APPROVAL STANDARD/EXPERT REVIEW PANELS FOR MINOR USES INVOLVING NON-FOOD ANIMALS

o Will animal caretakers find drugs approved under the proposed alternate standard (with associated restrictions) acceptable?

Yes, caretakers will recognize that adverse reactions may occur -as they do with drugs under the current rigorous process. However, this can be addressed by enhancing the reporting and communication process for addressing adverse reactions - perhaps using an electronic communication approach.

o Do the affected industries have the needed expertise and/or will they be willing to fund the expert review panels?

If this proposal is extended to food animals then the answer is yes, as long as the correct priorities are addressed, the producer association is involved in the process, and the solution demonstrably costs the industry less than the problem.

o Is the proposed process appropriately restricted to minor uses involving non-food animals?

This proposal could be pilot tested on non-food animals and then extended to food animals if successful. Careful selection of expert panel members to avoid potential charges of economic bias will be a key challenge. One concern is that a five year period is insufficient for completion of additional studies for a minor use proposal. A product sponsor seeking public funding may require two years to get a grant proposal refined and approved and then another year before the funding is actually available to undertake the research work. A better approach is to have an ongoing sunset option rather than a fixed period, such that the conditional approval could be withdrawn without evidence of an ongoing initiative to develop the required data.

I. INTERNATIONAL HARMONIZATION

- Could non-governmental input facilitate equivalency determinations?

Equivalency determination is best conducted by governments, although drug sponsors can provide valuable insight into issues that could be better managed through harmonization.

- Are there sufficient numbers of foreign approvals to justify establishing this program?

Yes, particularly in the field of aquaculture drugs.

- Should the proposed differences in approval, standards, processes, and data requirements between major and minor species be included in international harmonization activities?

Yes, in particular, any successful initiatives to support minor species drug approvals in other countries should be examined and the lessons learned from these programs should be brought back for adoption domestically.